

Title: IDENTIFICATION AND CHARACTERIZATION OF A
GENE WHICH PROTECTS CELLS FROM PROGRAMMED
CELL DEATH AND USES THEREFOR
Applicants: Horvitz et al.
Filing Date: November 6, 2001 Serial No.: 09/993,420
Customer No.: 21559

ced-9 genomic 930608 Sequence

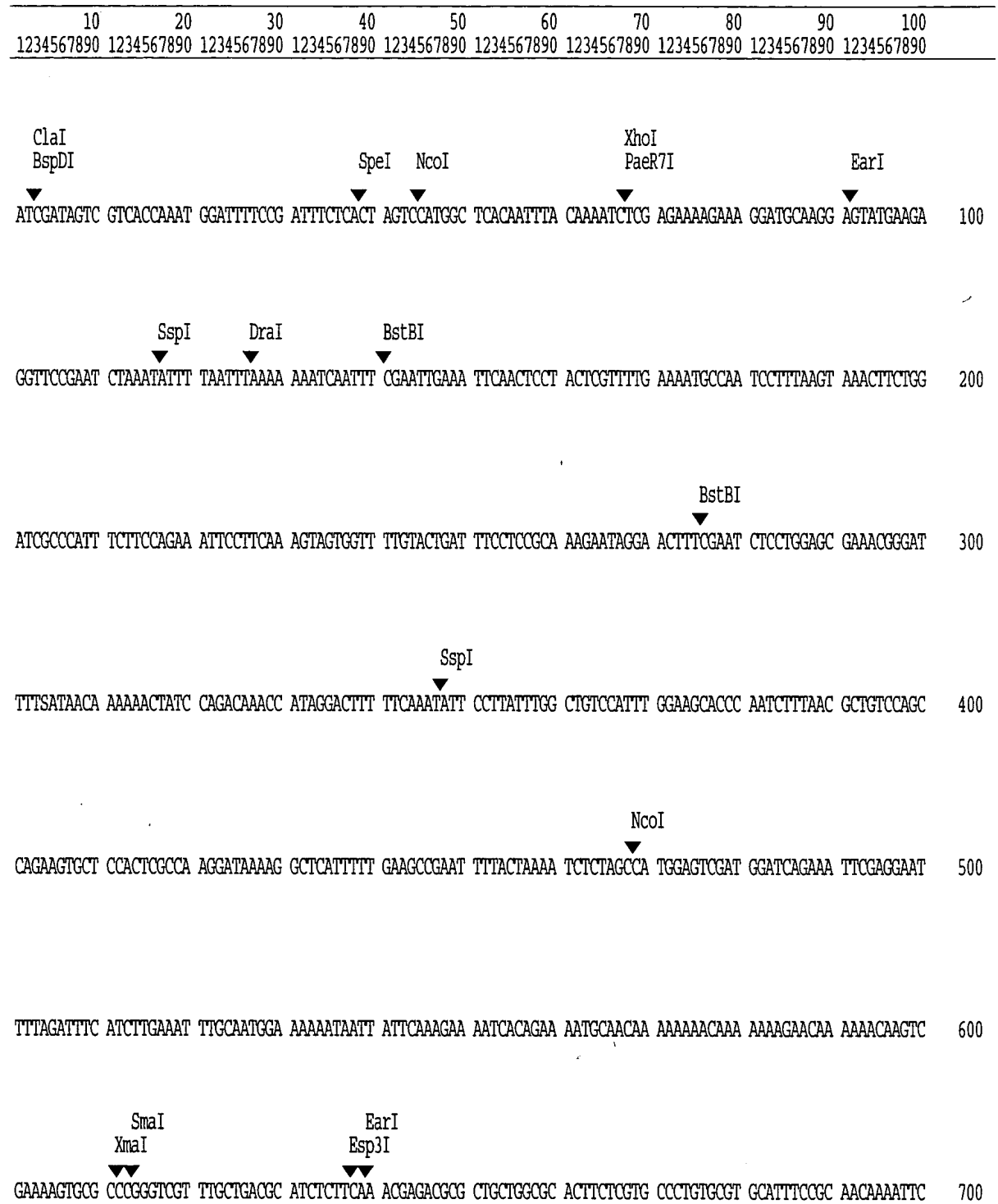


Fig. 2A



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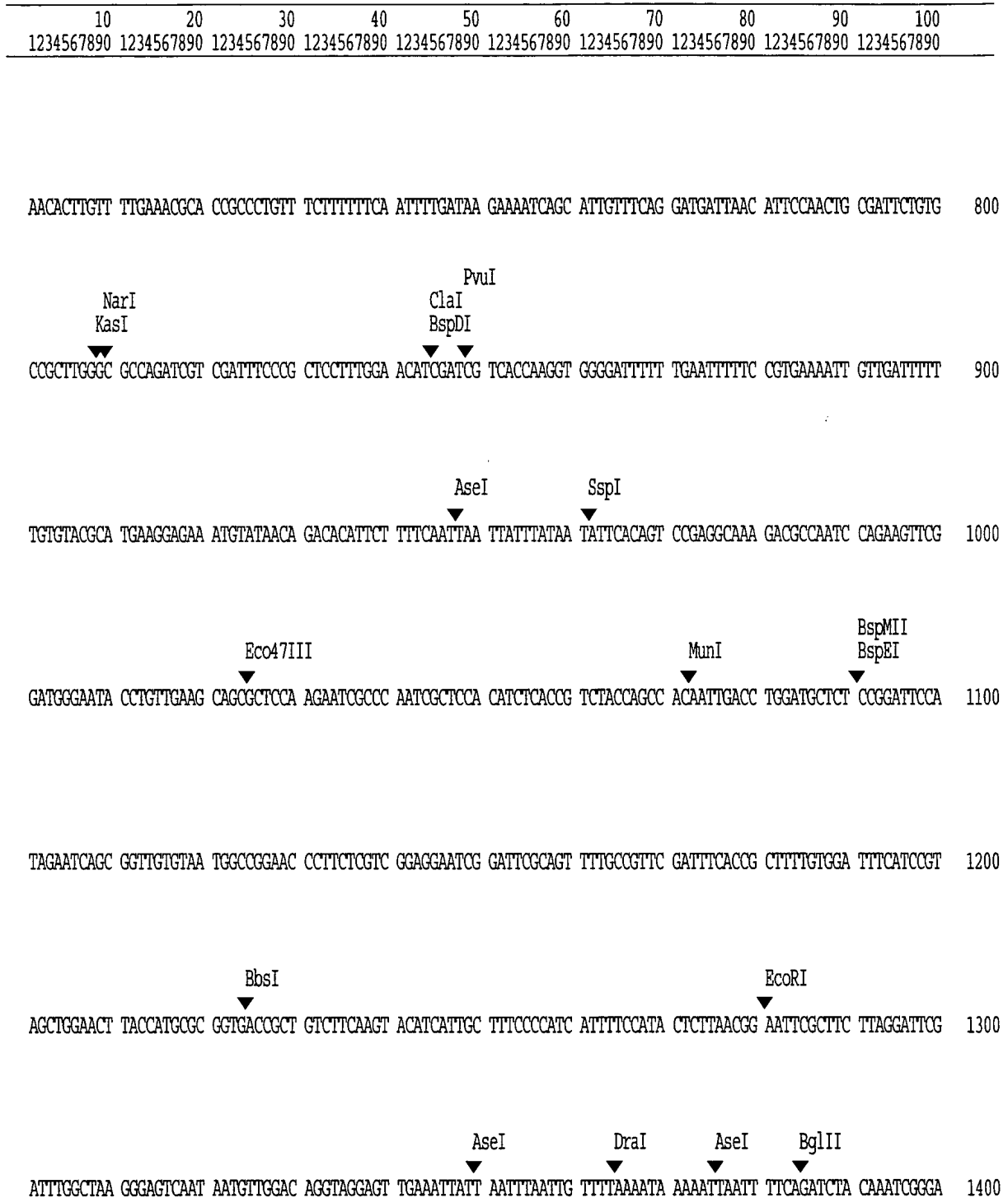


Fig. 2B

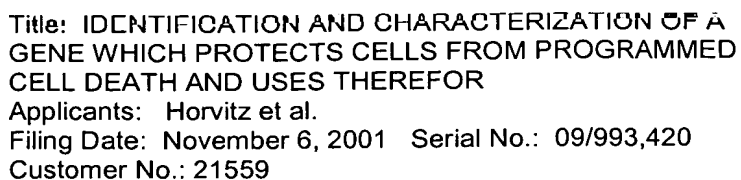
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Fig. 2C



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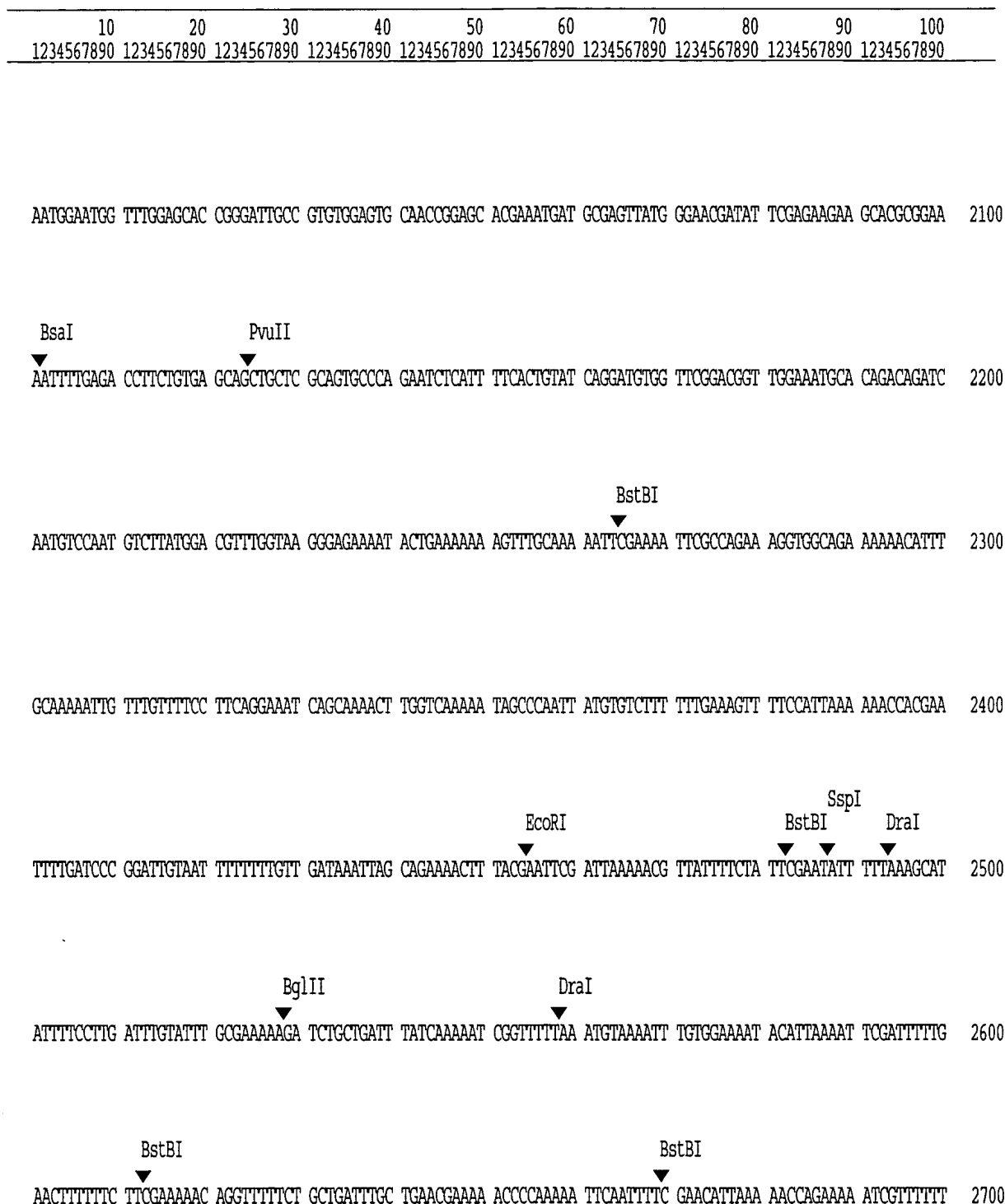


Fig. 2D



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HindIII
▼
TAAGCTTAAT TTTCGGCCAG AATGAACGA ATTAAATTGC AAATTTCTAA TTTTCAGATA GGTCTAATCT CGTTCGGCCG TTTCTAGCT GCAAAAATGA 2800

PstI EarI BamHI
▼ ▼ ▼
TGGAATCCGT GGAAGTGCAG GGACAAGTGC GAAACCTCTT CGTTTACACA TCGCTGTTCA TCAAAACGCG GATCCGCAAC AACTGGAAGG AACACAATCG 2900

SmaI
XmaI
▼ ▼
GAGCTGGGTA AGGAGTATTT GCATAGACAT TAGAAGTCAA TATCCCCCTT TCCCTAGTAC CCTTGACTTC CCGGGGTGTT GGTAAAGCCGA TAATTACAGG 3000

PvuII BsmI
▼ ▼
GTTCGGTAGC CTCTTGGGGG GACAGCTGGA AACATATTCA AGTATATTAC TGTATTATGAT AATGTTATTG TTACGGGAAT ACAAATTCG CAGAATGCTA 3100

DraI DraI
▼ ▼
TTTACAACA TATTTGACGC GCAAAATATC CAGTAGAGAA AACTACAGTA ATTCTTTAAA TTTTAAAAAT TTTTACAATT AAAGAAAATA ACCACTAATC 3200

AseI DraI
▼ ▼
AAAAGAAATT AATTTCAAAA ATCGAGCCCG TAAATCGACT ACASTAGGCA TTTAAAGAAT TACTGTAGTT TTGCTACGA GATATTTCCG CCTCAAATAT 3300

BsmI
▼
GTGTGGAAT ACGCATTCAC GGATTTTGT GTCCCGGA ATATGCTCTA AAGCATTATT TGTGAAAATA AAAAATCAAG AAAAAATTG CAGGACGACT 3400

Fig. 2E



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BspHI
▼
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PvuII
▼
TGGAGTAACA GCTGGAGCCA TTGGAATCGT TGGAGTCGTC GTGTGTGGGC GGATGATGTT CAGCTTGAAG TAACGTATTC AATTGTGTGA AATAATTAAAT 3600

AseI
▼
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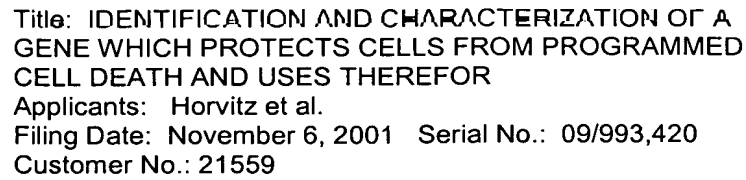
MscI
▼
TCGTGTGCGA TTACGATTTT TACTGCAATT TTTTCCGATT GCCTTTTTTT TTGGCCAAAC CCTACTTCCG CGTAATATCA ACTTTTCCGT GTTCTGTACA 3800

EarI
▼
TTTGTCAAA AACCTGAAA CCTAACTTT TCTGCGGTG GCCTAGCCTC CCGTCTCTCT TCCACATTTT CAAAGTACCC CTGTATCTCA ATAATTCATC 3900

SplI
BsiWI
EarI
MluI
▼
TTCACITTA A CTGTCTCTT TCGTGTGGCC TCTTCCAAT CCCCCCAAT TCCTGTACGC GTACGCGACT TTGTATTTAT TTTTTCAAA TTGTTTTCTC 4000

TCTACAACAA CAAAAAAAC GGTTCITTTA TTCAACCCIT TTTTCGGAAC GAAACTGCAA TTTTGATAAT AGCGGTGCGC AAGAGAATCC GGTTCITCATT 4100

Fig. 2F



10	20	30	40	50	60	70	80	90	100	
1234567890	1234567890	1234567890	1234567890	1234567890	1234567890	1234567890	1234567890	1234567890	1234567890	
							XhoI			
							PaeR7I			
							Esp3I			
							EarI			
TTCGCCATCA	CGTCATCCAA	AAAAGTTTAG	TAGGAAAATA	TCATTTTTTA	ATATAATGAT	TCATCTTTCT	CGCCTCTTCT	GTCTCGAGAC	GACGGTCAAT	
									4200	
		BstBI								
TCGATGCGCT	TGAATTTTTC	GAAAACAAAA	ATGTTTTTGT	TTAGTGTAAG	CGATCCCCCG	GCCTTATCGC	TGTTTCACCA	TCAGATAGGC	TCCGCCATTT	
									4300	
				ApaLI						
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									4400	
						EarI	EcoRI			
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									4500	
					StuI					
AGATACTCGT	GAGTTTTCAG	TCTTGTTTAG	CTTGAAACGG	CTTAAAAAGG	ACTAAAAAGG	CCTAAAAATT	GAAGTTTTC	ACCTGTTTTC	AAAAGAAAGC	
									4600	
CGAATTGCAC	AGCITTACAC	GAGATTCTCT	AATAATTGTG	ATTTGAAATT	TTCATATTCA	TCCCCAAAGC	TTCTTTACAC	GAAATTTTGC	GATTTTTCAG	
									4700	
		BsaI						DraI		
CTTAAATAC	GATACCTGGT	CTCGACACGA	AACATTTTTC	TTAAATTCAA	AAAGATGTGC	GCCTTTAAAG	AGTGTCTGTAG	TTTGAAACTT	CTGTGTGTGC	
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Fig. 2G

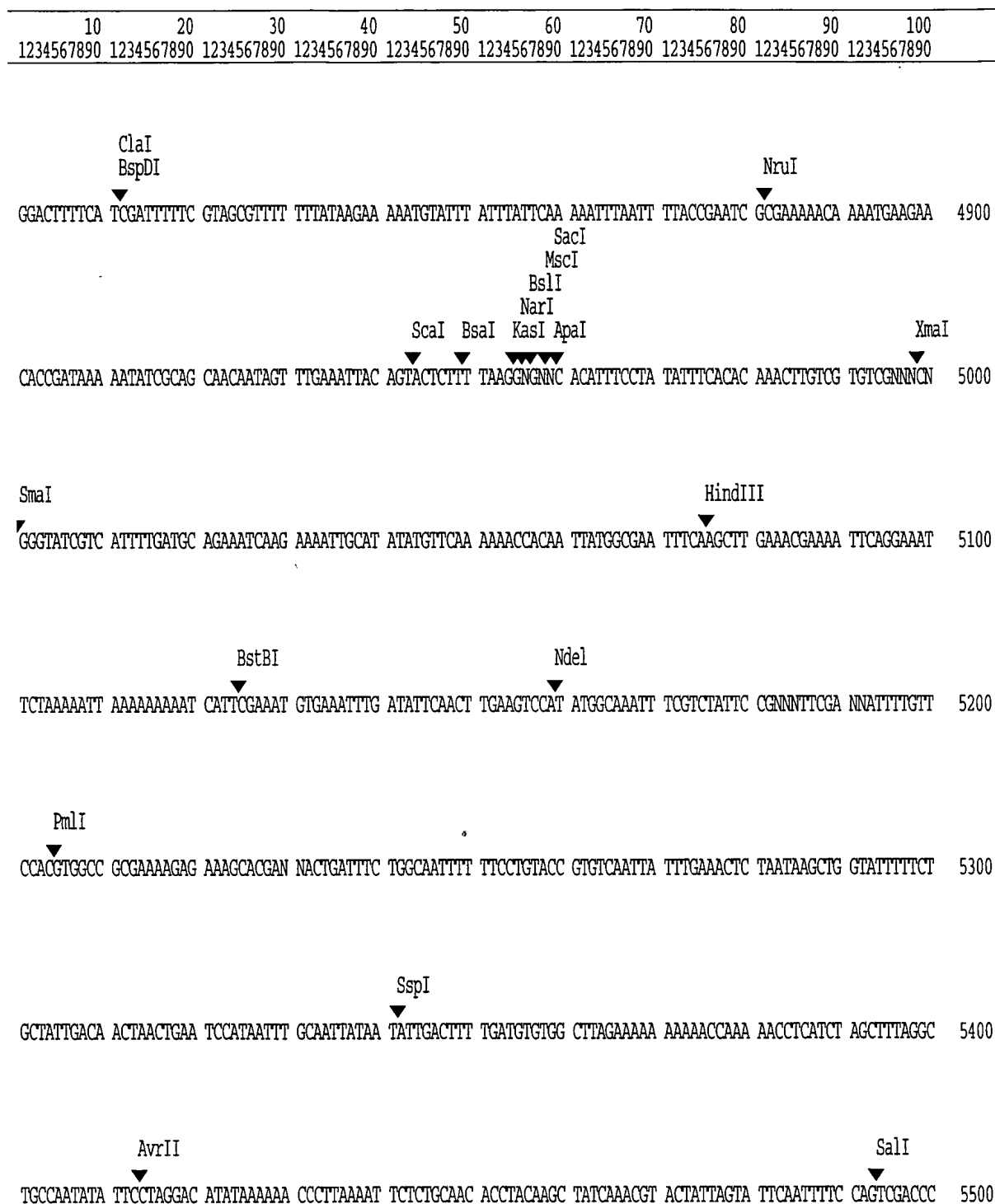
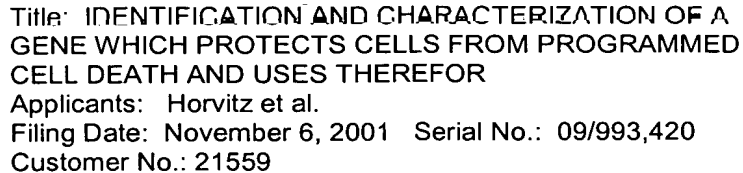


Fig. 2H



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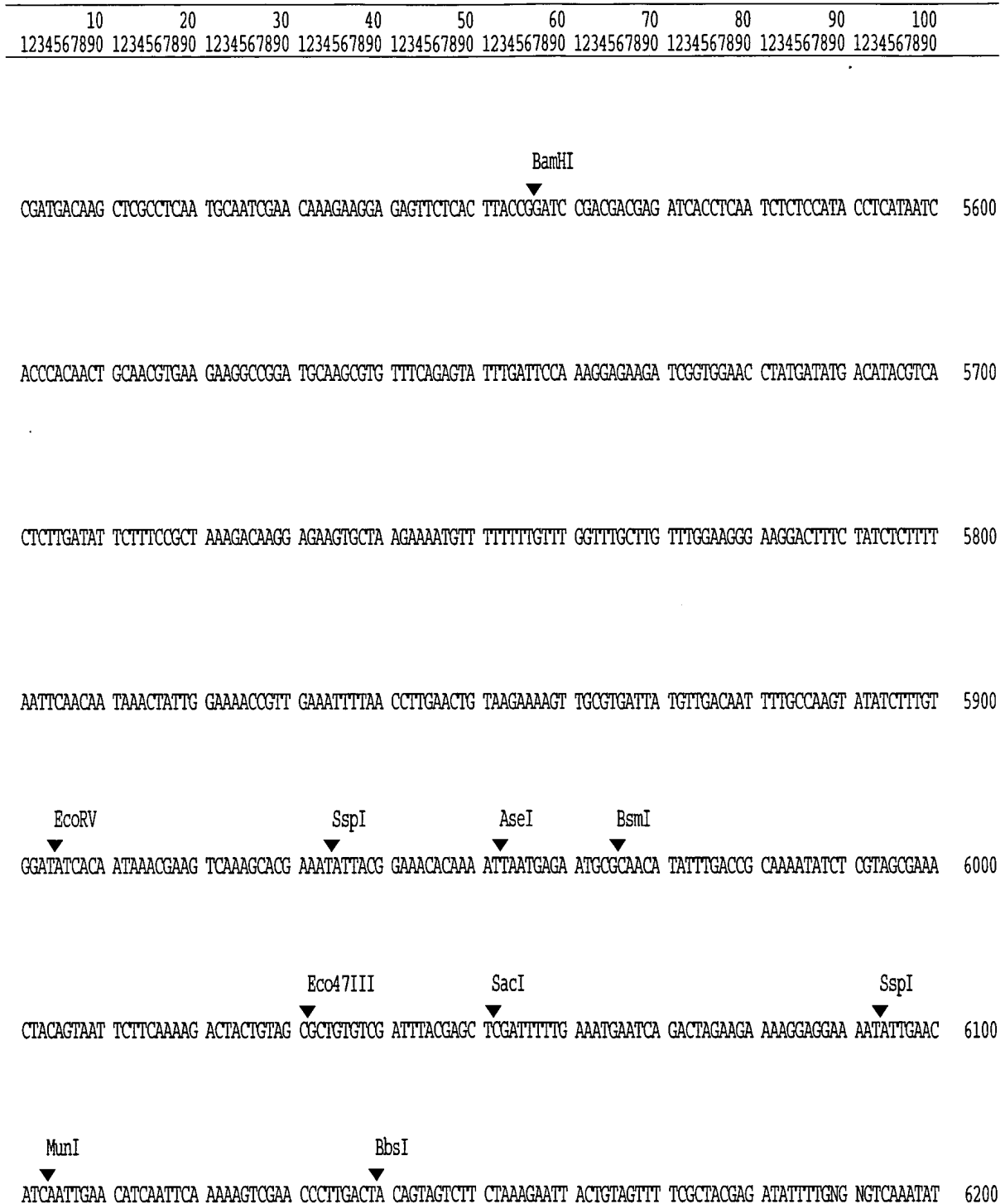


Fig. 21

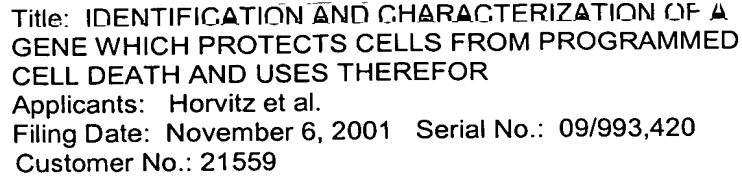
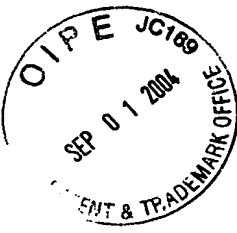
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Fig. 2J



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1 GCGCCCGCCC CTCCGCGCCG CCTGCCCCGCC CGCCCGCCGC GCTCCCGCCC
51 GCCGCTCTCC GTGGCCCCGC CGCGCTGCCG CCGCCGCCGC TGCCAGCGAA
101 GGTGCCGGGG CTCCGGGCCC TCCCTGCCGG CGGCCGTCAG CGCTCGGAGC
151 GAACTGCGCG ACGGGAGGTC CGGGAGGCGA CCGTAGTCGC GCCGCCGCGC
201 AGGACCAGGA GGAGGAGAAA GGGTGCGCAG CCCGGAGGCG GGGTGCGCCG
251 GTGGGGTGCA GCGGAAGAGG GGGTCCAGGG GGGAGAACTT CGTAGCAGTC
301 ATCCTTTTTA GGAAAAGAGG GAAAAAATAA AACCTCCCC CACCACCTCC
351 TTCTCCCCAC CCCTCGCCGC ACCACACACA GCGCGGGCTT CTAGCGCTCG
401 GCACCGGCGG GCCAGGCGCG TCCTGCCTTC ATTTATCCAG CAGCTTTTCG
451 GAAAATGCAT TTGCTGTTCG GAGTTTAATC AGAAGACGAT TCCTGCCTCC

Fig. 7A



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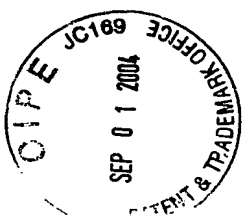
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551 CGTGAAGCGG TCCCGTGGAT AGAGATTCAT GCCTGTGTCC GCGCGTGTGT
601 GCGCGCGTAT AAATTGCCGA GAAGGGGAAA ACATCACAGG ACTTCTGCGA
651 ATACCGGACT GAAAATTGTA ATTCATCTGC CGCCGCCGCT GCCAAAAAAA
701 AACTCGAGCT CTTGAGATCT CCGGTTGGGA TTCCTGCGGA TTGACATTTT
751 TGTGAAGCAG AAGTCTGGGA ATCGATCTGG AAATCCTCCT AATTTTTACT
801 CCCTCTCCCC CCGACTCCTG ATTCATTGGG AAGTTTCAAA TCAGCTATAA
851 CTGGAGAGTG CTGAAGATTG ATGGGATCGT TGCCTTATGC ATTTGTTTTG
901 GTTTTACAAA AAGGAACTT GACAGAGGAT CATGCTGTAC TTAaaaaata
951 CAAGTAAGTC TCGCACAGGA AATTGGTTTA ATGTAACTTT CAATGGAAAC
1001 CTTTGAGATT TTTTACTTAA AGTGCATTCT AGTAAATTTA ATTTCCAGGC
1051 AGCTTAATAC ATTGTTTTTA GCCGTGTTAC TTGTAGTGTG TATGCCCTGC
1101 TTTCACCTCAG TGTGTACAGG GAAACGCACC TGATTTTTTA CTTATTAGTT
1151 TGTTTTTTTCT TTAACCTTTC AGCATCACAG AGGAAGTAGA CTGATATTAA
1201 CAATACTTAC TAATAATAAC GTGCCTCATG AAATAAAGAT CCGAAAGGAA
1251 TTGGAATAAA AATTTCTGTC GTCTCATGCC AAGAGGGAAA CACCAGAATC
1301 AAGTGTTCCG CGTGATTGAA GACACCCCTT CGTCCAAGAA TGCAAAGCAC
1351 ATCCAATAAA ATAGCTGGAT TATAACTCCT CTTCTTTCTC TGGGGGCCGT
1401 GGGGTGGGAG CTGGGGCGAG AGGTGCCGTT GGCCCCCGTT GCTTTTCCTC
1451 TGGGAAGGAT GGCGCACGCT GGGAGAACGG GGTACGACAA CCGGGAGATA
1501 GTGATGAAGT ACATCCATTA TAAGCTGTCG CAGAGGGGCT ACGAGTGGGA
1551 TGCGGGAGAT GTGGGCGCCG CGCCCCCGGG GGCCGCCCCC GCACCGGGCA
1601 TCTTCTCCTC CCAGCCCGGG CACACGCCCC ATCCAGCCGC ATCCGCGAC
1651 CCGGTCGCCA GGACCTCGCC GCTGCAGACC CCGGCTGCCC CCGGCGCCGC
1701 CGCGGGGCCT GCGCTCAGCC CGGTGCCACC TGTGGTCCAC CTGGCCCTCC
1751 GCCAAGCCGG CGACGACTTC TCCCGCCGCT ACCGCGGCGA CTTGCGCCGAG
1801 ATGTCCAGCC AGCTGCACCT GACGCCCTTC ACCGCGCGGG GACGCTTTGC
1851 CACGGTGGTG GAGGAGCTCT TCAGGGACGG GGTGAACTGG GGGAGGATTG
1901 TGGCCTTCTT TGAGTTCGGT GGGGTCATGT GTGTGGAGAG CGTCAACCGG

Fig. 7B



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1951 GAGATGTCGC CCCTGGTGGG CAACATCGCC CTGTGGATGA CTGAGTACCT
2001 GAACCGGCAC CTGCACACCT GGATCCAGGA TAACGGAGGC TGGGATGCCT
2051 TTGTGGAACGT GTACGGCCCC AGCATGCGGC CTCTGTTTGA TTTCTCCTGG
2101 CTGTCTCTGA AGACTCTGCT CAGTTTGGCC CTGGTGGGAG CTTGCATCAC
2151 CCTGGGTGCC TATCTGAGCC ACAAGTGAAG TCAACATGCC TGCCCCAAAC
2201 AAATATGCAA AAGGTTCACT AAAGCAGTAG AAATAATATG CATTGTCAGT
2251 GATGTACCAT GAAACAAAGC TGCAGGCTGT TTAAGAAAAA ATAACACACA
2301 TATAAACATC ACACACACAG ACAGACACAC ACACACACAA CAATTAACAG
2351 TCTTCAGGCA AAACGTCGAA TCAGCTATTT ACTGCCAAAG GGAAATATCA
2401 TTTATTTTTT ACATTATTAA GAAAAAAGAT TTATTTATTT AAGACAGTCC
2451 CATCAAAACT CCGTCTTTGG AAATCCGACC ACTAATTGCC AAACACCGCT
2501 TCGTGTGGCT CCACCTGGAT GTTCTGTGCC TGTAAACATA GATTGCTTTT
2551 CCATGTTGTT GGCCGGATCA CCATCTGAAG AGCAGACGGA TGGAAAAAGG
2601 ACCTGATCAT TGGGGAAGCT GGCTTTCTGG CTGCTGGAGG CTGGGGAGAA
2651 GGTGTTTATT CACTTGCATT TCTTTGCCCT GGGGGCGTGA TATTAACAGA
2701 GGGAGGGTTC CCGTGGGGGG AAGTCCATGC CTCCCTGGCC TGAAGAAGAG
2751 ACTCTTTGCA TATGACTCAC ATGATGCATA CCTGGTGGGA GGAAAAGAGT
2801 TGGGAACTTC AGATGGACCT AGTACCCACT GAGATTTCCTA CGCCGAAGGA
2851 CAGCGATGGG AAAAATGCCC TTAAATCATA GGAAAGTATT TTTTAAAGCT
2901 ACCAATTGTG CCGAGAAAAG CATTTTAGCA ATTTATACAA TATCATCCAG
2951 TACCTTAAAC CCTGATTGTG TATATTCATA TATTTTGGAT ACGCACCCCC
3001 CAACTCCCAA TACTGGCTCT GTCTGAGTAA GAAACAGAAT CCTCTGGAAC
3051 TTGAGGAAGT GAACATTTCTG GTGACTTCCG ATCAGGAAGG CTAGAGTTAC
3101 CCAGAGCATC AGGCCGCCAC AAGTGCCTGC TTTTAGGAGA CCGAAGTCCG
3151 CAGAACCTAC CTGTGTCCCA GCTTGGAGGC CTGGTCCTGG AACTGAGCCG
3201 GGCCCTCACT GGCCCTCTCC AGGGATGATC AACAGGGTAG TGTGGTCTCC
3251 GAATGTCTGG AAGCTGATGG ATGGAGCTCA GAATTCCACT GTCAAGAAAG
3301 AGCAGTAGAG GGGTGTGGCT GGGCCTGTCA CCCTGGGGCC CTCCAGGTAG
3351 GCCCGTTTTT ACGTGGAGCA TAGGAGCCAC GACCCTTCTT AAGACATGTA

Fig. 7C



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3401 TCACTGTAGA GGAAGGAAC AGAGGCCCTG GGCCTTCCTA TCAGAAGGAC
3451 ATGGTGAAGG CTGGGAACGT GAGGAGAGGC AATGGCCACG GCCCATTTTG
3501 GCTGTAGCAC ATGGCACGTT GGCTGTGTGG CCTTGGCCAC CTGTGAGTTT
3551 AAAGCAAGGC TTAAATGAC TTTGGAGAGG GTCACAAATC CTAAAAGAAG
3601 CATTGAAGTG AGGTGTCATG GATTAATTGA CCCCTGTCTA TGGAATTACA
3651 TGTA AACAT TATCTTGTC CTGTAGTTTG GTTTTATTTG AAAACCTGAC
3701 AAAAAAAAAAG TTCCAGGTGT GGAATATGGG GGTTATCTGT ACATCCTGGG
3751 GCATTAAAAA AAAATCAATG GTGGGGAACT ATAAAGAAGT AACAAAAGAA
3801 GTGACATCTT CAGCAAATAA ACTAGGAAAT TTTTTTTTCT TCCAGTTTAG
3851 AATCAGCCTT GAAACATTGA TGGAATAACT CTGTGGCATT ATTGCATTAT
3901 ATACCATTTA TCTGTATTAA CTTTGGAATG TACTCTGTTC AATGTTTAAT
3951 GCTGTGGTTG ATATTTTCGAA AGCTGCTTTA AAAAAATACA TGCATCTCAG
4001 CGTTTTTTTTG TTTTAAATTG TATTTAGTTA TGGCCTATAC ACTATTTGTG
4051 AGCAAAGGTG ATCGTTTTCT GTTTGAGATT TTTATCTCTT GATTCTTCAA
4101 AAGCATTCTG AGAAGGTGAG ATAAGCCCTG AGTCTCAGCT ACCTAAGAAA
4151 AACCTGGATG TCACTGGCCA CTGAGGAGCT TTGTTTCAAC CAAGTCATGT
4201 GCATTTCCAC GTCAACAGAA TTGTTTATTG TGACAGTTAT ATCTGTTGTC
4251 CCTTTGACCT TGTTTCTTGA AGGTTTCCTC GTCCCTGGGC AATTCCGCAT
4301 TTAATTCATG GTATTCAGGA TTACATGCAT GTTTGGTTAA ACCCATGAGA
4351 TTCATTCAGT TAAAAATCCA GATGGCGAAT GACCAGCAGA TTCAAATCTA
4401 TGGTGGTTTG ACCTTTAGAG AGTTGCTTTA CGTGGCCTGT TTCAACACAG
4451 ACCCACCCAG AGCCCTCCTG CCCTCCTTCC GCGGGGGCTT TCTCATGGCT
4501 GTCCTTCAGG GTCTTCCTGA AATGCAGTGG TCGTTACGCT CCACCAAGAA
4551 AGCAGGAAAC CTGTGGTATG AAGCCAGACC TCCCCGGCGG GCCTCAGGGA
4601 ACAGAATGAT CAGACCTTTG AATGATTCTA ATTTTAAAGC AAAATATTAT
4651 TTTATGAAAG GTTTACATTG TCAAAGTGAT GAATATGGAA TATCCAATCC
4701 TGTGCTGCTA TCCTGCCAAA ATCATTTTAA TGGAGTCAGT TTGCAGTATG
4751 CTCCACGTGG TAAGATCCTC CAAGCTGCTT TAGAAGTAAC AATGAAGAAC
4801 GTGGACGTTT TTAATATAAA GCCTGTTTTG TCTTTTGTTG TTGTTCAAAC

Fig. 7D



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4851 GGGATTCA CA GAGTATTTGA AAAATGTATA TATATTAAGA GGTCACGGGG
4901 GCTAATTGCT AGCTGGCTGC CTTTGTCTGT GGGGTTTTGT TACCTGGTTT
4951 TAATAACAGT AAATGTGCCC AGCCTCTTGG CCCCAGAACT GTACAGTATT
5001 GTGGCTGCAC TTGCTCTAAG AGTAGTTGAT GTTGCATTTT CTTATTGTT
5051 AAAAACATGT TAGAAGCAAT GAATGTATAT AAAAGC

Fig. 7E



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n3400

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M T R C T A D N S L T N P A Y R R R T M

40
GCG ACT GGC GAG ATG AAG GAG TTT CTG GGG ATA AAA GGC ACA GAG CCC ACC GAT TTT GGA
A T G E M K E F L G I K G T E P T D F G
T n2812 Q46Amber

60
ATC AAT AGT GAT GCT CAG GAC TTG CCA TCA CCG AGT AGG CAG GCT TCG ACG CGA AGA ATG
I N S D A Q D L P S P S R Q A S T R R M

80
TCC ATC GGA GAG TCA ATT GAT GGA AAA ATC AAT GAT TGG GAA GAG CCA AGG CTT GAT ATC
S I G E S I D G K I N D W E E P R L D I
A n3377 E74K

100
GAG GGA TTT GTG GTC GAC TAT TTC ACG CAC CGA ATC CCG CAA AAC GGA ATG GAA TGG TTT
E G F V V D Y F T H R I R Q N G M E W F

BH4

120
GGA GCA CCG GGA TTG CCG TGT GGA GTG CAA CCG GAG CAC GAA ATG ATG CGA GTT ATG GGA
G A P G L P C G V Q P E H E M M R V M G

BH3

140
ACG ATA TTC GAG AAG AAG CAC GCG GAA AAT TTT GAG ACC TTC TGT GAG CAG CTG CTC GCA
T I F E K K H A E N F E T F C E Q L L A

A n1653 Y149N n2077 Q160Amber T

160
GTG CCC AGA ATC TCA TTT TCA CTG TAT CAG GAT GTG GTT CCG ACG GTT GGA AAT GCA CAG
V P R I S F S L Y Q D V V R T V G N A Q

n1950 G169E A n3407 splice acceptor

180
ACA GAT CAA TGT CCA ATG TCT TAT GGA CGT TTG ATA GGT CTA ATC TCG TTC GGC GGT TTC
T D Q C P M S Y G R L I G L I S F G G F

BH1

200
GTA GCT GCA AAA ATG ATG GAA TCC GTG GAA CTG CAG GGA CAA GTG CGA AAC CTC TTC GTT
V A A K M M E S V E L Q G Q V R N L F V

220
TAC ACA TCG CTG TTC ATC AAA ACG CGG ATC CGC AAC AAC TGG AAG GAA CAC AAT CGG AGC
Y T S L F I K T R I R N N W K E H N R S

BH2

240
TGG GAC GAC TTC ATG ACA CTC GGA AAA CAA ATG AAA GAG GAC TAC GAA CGA GCA GAA GCT
W D D F M T L G K Q M K E D Y E R A E A

260
GAA AAA GTG GGA CGC CGG AAG CAG AAC AGA CGG TGG TCG ATG ATT GGC GCT GGA GTA ACA
E K V G R R K Q N R R W S M I G A G V T

280
GCT GGA GCC ATT GGA ATC GTT GGA GTC GTC GTG TGT GGG CGG ATG ATG TTC AGC TTG AAG
A G A I G I V G V V C G R M M F S L K

Fig. 11